

What is claimed is:

1. A stabilized radiopharmaceutical composition comprising:
 - (a) a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and
 - (b) a stabilizer comprising a water-soluble organic compound containing selenium in the +2 oxidation state.

5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130 135 140 145 150 155 160 165 170 175 180 185 190 195 200 205 210 215 220 225 230 235 240 245 250 255 260 265 270 275 280 285 290 295 300 305 310 315 320 325 330 335 340 345 350 355 360 365 370 375 380 385 390 395 400 405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585 590 595 600 605 610 615 620 625 630 635 640 645 650 655 660 665 670 675 680 685 690 695 700 705 710 715 720 725 730 735 740 745 750 755 760 765 770 775 780 785 790 795 800 805 810 815 820 825 830 835 840 845 850 855 860 865 870 875 880 885 890 895 900 905 910 915 920 925 930 935 940 945 950 955 960 965 970 975 980 985 990 995 1000 1005 1010 1015 1020 1025 1030 1035 1040 1045 1050 1055 1060 1065 1070 1075 1080 1085 1090 1095 1100 1105 1110 1115 1120 1125 1130 1135 1140 1145 1150 1155 1160 1165 1170 1175 1180 1185 1190 1195 1200 1205 1210 1215 1220 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11005 11010 11015 11020 11025 11030 11035 11040 11045 11050 11055 11060 11065 11070 11075 11080 110

(b) a stabilizer comprising a water-soluble organic compound containing selenium in the +2 oxidation state.

8. A stabilized radiopharmaceutical composition of claim 7, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenomethionine or a derivative thereof.

9. A stabilized radiopharmaceutical composition of claim 7, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenocysteine or a derivative thereof.

10. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



15 wherein

M is a metal chelator complexed with a radionuclide;

N is 0, an alpha amino acid, a non-alpha amino acid, or other linking group;

O is an alpha amino acid, or a non-alpha amino acid;

20 P is 0, an alpha amino acid, a non-alpha amino acid, or other linking group; and

Q is a targeting molecule;

wherein at least one of N, O or P is a non-alpha amino acid; and

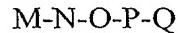
25 (b) a stabilizer comprising a water-soluble organic compound containing selenium in the +2 oxidation state.

11. A stabilized radiopharmaceutical composition of claim 10, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenomethionine or a derivative thereof.

30 12. A stabilized radiopharmaceutical composition of claim 10, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenocysteine or a derivative thereof.

35 13. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

M is a metal chelator complexed with a radionuclide;

5 N is O, an alpha amino acid, a substituted bile acid, or other linking group;

O is an alpha amino acid, or a substituted bile acid;

P is O, an alpha amino acid, a substituted bile acid, or other linking group; and

10 Q is a targeting molecule;

wherein at least one of N, O or P is a substituted bile acid; and

(b) a stabilizer comprising a water-soluble organic compound containing selenium in the +2 oxidation state.

15 14. A stabilized radiopharmaceutical composition of claim 13, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenomethionine or a derivative thereof.

20 15. A stabilized radiopharmaceutical composition of claim 13, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenocysteine or a derivative thereof.

25 16. A stabilized radiopharmaceutical composition of claims 1-15, wherein the metal chelator is selected from the group consisting of DTPA, DOTA, DO3A, HP-DO3A, PA-DOTA, MeO-DOTA, MX-DTPA, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM, MECAM, CMDOTA, PnAO, oxa-PnAO, N,N-dimethylGly-Ser-Cys; N,N-dimethylGly-Thr-Cys; N,N-diethylGly-Ser-Cys; N,N-dibenzylGly-Ser-Cys, N,N-dimethylGly-Ser-Cys-Gly; N,N-dimethylGly-Thr-Cys-Gly ; N,N-diethylGly-Ser-Cys-Gly; and N,N-dibenzylGly-Ser-Cys-Gly.

30 17. A stabilized radiopharmaceutical composition of claims 1-15, wherein the targeting molecule is a targeting peptide.

35 18. A stabilized radiopharmaceutical composition of claim 17, wherein the targeting peptide is selected from the group consisting of LHRH, insulin, oxytocin,

somatostatin, NK-1, VIP, Substance P, NPY, endothelin A, endothelin B, bradykinin, interleukin-1, EGF, CCK, galanin, MSH, Lanreotide, Octreotide, Maltose, arginine-vasopressin and analogs and derivatives thereof.

5 19. A stabilized radiopharmaceutical composition of claim 17, wherein the targeting peptide is LHRH or an analog thereof.

20. A stabilized radiopharmaceutical composition of claim 17, wherein the targeting molecule is a GRP receptor targeting molecule or an analog thereof.

10 21. A stabilized radiopharmaceutical composition of claim 20, wherein the GRP receptor targeting molecule is an agonist or a peptide which confers agonist activity.

15 22. A stabilized radiopharmaceutical composition of claim 20, wherein the GRP receptor targeting molecule is bombesin or an analog thereof.

20 23. A stabilized radiopharmaceutical composition of claim 1-15, wherein the radionuclide is selected from the group consisting of ^{99m}Tc , ^{51}Cr , ^{67}Ga , ^{68}Ga , ^{47}Sc , ^{167}Tm , ^{141}Ce , ^{123}I , ^{125}I , ^{131}I , ^{18}F , ^{11}C , ^{15}N , ^{111}In , ^{168}Yb , ^{175}Yb , ^{140}La , ^{90}Y , ^{88}Y , ^{86}Y , ^{153}Sm , ^{166}Ho , ^{165}Dy , ^{166}Dy , ^{62}Cu , ^{64}Cu , ^{67}Cu , ^{97}Ru , ^{103}Ru , ^{186}Re , ^{188}Re , ^{203}Pb , ^{211}Bi , ^{212}Bi , ^{213}Bi , ^{214}Bi , ^{225}Ac , ^{211}At , ^{105}Rh , ^{109}Pd , ^{117m}Sn , ^{149}Pm , ^{161}Tb , ^{177}Lu , ^{198}Au and ^{199}Au and oxides or nitrides thereof.

25 24. A stabilized radiopharmaceutical composition comprising:

(a) a diagnostic or therapeutic radionuclide, optionally complexed to a

chelator; and

(b) a stabilizer composition which comprises ascorbic acid or a pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

30 25. A stabilized radiopharmaceutical composition comprising:

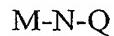
(a) a metal chelator complexed with a radionuclide;

(b) an optional linking group and a targeting molecule; and

(c) a stabilizer composition which comprises ascorbic acid or a pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

26. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

5 M is a metal chelator complexed with a radionuclide;

N is an optional linker; and

Q is a targeting molecule; and

(b) a stabilizer composition which comprises ascorbic acid or a

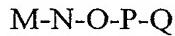
pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

27. A stabilized radiopharmaceutical composition of claim 26, wherein the linking group is a hydrocarbon linking group.

15 28. A stabilized radiopharmaceutical composition of claim 27, wherein the linking group is aminovaleric acid.

29. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

M is a metal chelator complexed with a radionuclide;

N is 0, an alpha amino acid, a non-alpha amino acid, or other linking group;

25 O is an alpha amino acid, or a non-alpha amino acid;

P is 0, an alpha amino acid, a non-alpha amino acid, or other linking group; and

Q is a targeting molecule;

wherein at least one of N, O or P is a non-alpha amino acid; and

30 (b) a stabilizer composition which comprises ascorbic acid or a pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

30. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

M is a metal chelator complexed with a radionuclide;

5 N is O, an alpha amino acid, a substituted bile acid, or other linking group;

O is an alpha amino acid, or a substituted bile acid;

P is O, an alpha amino acid, a substituted bile acid, or other linking group; and

10 Q is a targeting molecule;

wherein at least one of N, O or P is a substituted bile acid; and

(b) a stabilizer composition which comprises ascorbic acid or a

pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

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31. A stabilized radiopharmaceutical composition of any of claims 24-30, wherein the stabilizer composition further comprises selenomethionine or a derivative thereof.

20 32. A stabilized radiopharmaceutical composition of any of claims 24-30, wherein the stabilizer composition further comprises selenocysteine or a derivative thereof.

33. A stabilized radiopharmaceutical composition of any of claims 24-30, wherein the stabilizer composition further comprises methionine or a derivative thereof.

25 34. A stabilized radiopharmaceutical composition of any of claims 24-30, wherein the stabilizer composition further comprises cysteine or a derivative thereof.

35. A stabilized radiopharmaceutical composition of claims 24-35, wherein the metal chelator is selected from the group consisting of DTPA, DOTA, DO3A, HP-DO3A, PA-DOTA, MeO-DOTA, MX-DTPA, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM, MECAM, CMDOTA, PnAO, oxa-PnAO, N,N-dimethylGly-Ser-Cys; N,N-dimethylGly-Thr-Cys; N,N-diethylGly-Ser-Cys; N,N-dibenzylGly-Ser-Cys, N,N-dimethylGly-Ser-Cys-Gly; N,N-dimethylGly-Thr-Cys-Gly ; N,N-diethylGly-Ser-Cys-Gly; and N,N-dibenzylGly-Ser-Cys-Gly.

36. A stabilized radiopharmaceutical composition of claims 24-35, wherein the targeting molecule is a targeting peptide.

5 37. A stabilized radiopharmaceutical composition of claim 36, wherein the targeting peptide is selected from the group consisting of LHRH, insulin, oxytocin, somatostatin, NK-1, VIP, Substance P, NPY, endothelin A, endothelin B, bradykinin, interleukin-1, EGF, CCK, galanin, MSH, Lanreotide, Octreotide, Maltose, arginine-vasopressin and analogs and derivatives thereof.

10 38. A stabilized radiopharmaceutical composition of claim 36, wherein the targeting peptide is LHRH or an analog thereof.

15 39. A stabilized radiopharmaceutical composition of claim 36, wherein the targeting molecule is a GRP receptor targeting molecule or an analog thereof.

40. A stabilized radiopharmaceutical composition of claim 36, wherein the GRP receptor targeting molecule is an agonist or a peptide which confers agonist activity.

20 41. A stabilized radiopharmaceutical composition of claim 36, wherein the GRP receptor targeting molecule is bombesin or an analog thereof.

42. A stabilized radiopharmaceutical composition of claims 24-41, wherein the radionuclide is selected from the group consisting of ^{99m}Tc , ^{51}Cr , ^{67}Ga , ^{68}Ga , ^{47}Sc , ^{167}Tm , ^{141}Ce , ^{123}I , ^{125}I , ^{131}I , ^{18}F , ^{11}C , ^{15}N , ^{111}In , ^{168}Yb , ^{175}Yb , ^{140}La , ^{90}Y , ^{88}Y , ^{86}Y , ^{153}Sm , ^{166}Ho , ^{165}Dy , ^{166}Dy , ^{62}Cu , ^{64}Cu , ^{67}Cu , ^{97}Ru , ^{103}Ru , ^{186}Re , ^{188}Re , ^{203}Pb , ^{211}Bi , ^{212}Bi , ^{213}Bi , ^{214}Bi , ^{225}Ac , ^{211}At , ^{105}Rh , ^{109}Pd , ^{117m}Sn , ^{149}Pm , ^{161}Tb , ^{177}Lu , ^{198}Au and ^{199}Au and oxides or nitrides thereof.

43. A stabilized radiopharmaceutical composition comprising:

30 (a) a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and
(b) a stabilizer comprising a dithiocarbamate compound.

44. A stabilized radiopharmaceutical composition comprising:

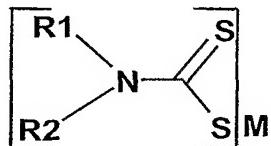
35 (a) a compound comprising a metal chelator complexed with a radionuclide;

- (b) an optional linking group and a targeting molecule; and
- (c) a stabilizer comprising a dithiocarbamate compound.

45. A stabilized radiopharmaceutical composition of claim 44, wherein the linking group is a hydrocarbon linking group.

46. A stabilized radiopharmaceutical composition of claim 45, wherein the linking group is aminovaleric acid.

47. A stabilized radiopharmaceutical composition of claim 43 or 44 wherein the dithiocarbamate compound has the formula:



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wherein R1 and R2 are each independently H; C₁-C₈ alkyl; -OR₃, wherein R₃ is C₁-C₈ alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

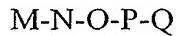
20 wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is H⁺, Na⁺, K⁺, NH₄⁺, N-methylglucamine, or other pharmaceutically acceptable +1 ion.

25 48. A stabilized radiopharmaceutical composition comprising a compound of claim 47, wherein the stabilizer compound is selected from the group consisting of 1-pyrrolidine dithiocarbamic acid ammonium salt, Sodium diethyldithiocarbamate trihydrate, Sodium dimethyldithiocarbamate hydrate, and combinations thereof.

30 49. A stabilized radiopharmaceutical composition comprising a compound of claim 48, wherein the stabilizer compound is 1-pyrrolidine dithiocarbamic acid ammonium salt.

50. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

5 M is a metal chelator complexed with a radionuclide;

N is O, an alpha amino acid, a non-alpha amino acid, or other linking group;

O is an alpha amino acid, or a non-alpha amino acid;

10 P is O, an alpha amino acid, a non-alpha amino acid, or other linking group; and

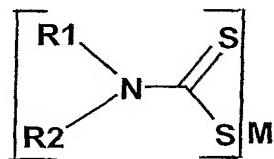
Q is a targeting molecule;

wherein at least one of N, O or P is a non-alpha amino acid; and

(b) a stabilizer comprising a dithiocarbamate compound.

15 51. A stabilized radiopharmaceutical composition of claim 50 wherein the

dithiocarbamate compound has the formula:

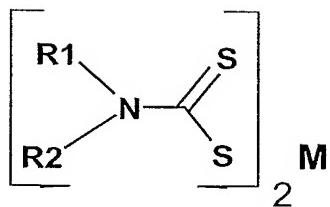


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wherein R1 and R2 are each independently H; C₁-C₈ alkyl; -OR₃, wherein R₃ is C₁-C₈ alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

25 wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is H⁺, Na⁺, K⁺, NH₄⁺, N-methylglucamine, or other pharmaceutically acceptable +1 ion.

30 52. A stabilized radiopharmaceutical composition of claim 50 wherein the dithiocarbamate compound has the formula:



wherein R1 and R2 are each independently H; C₁-C₈ alkyl; -OR₃, wherein R₃ is C₁-C₈ alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is Mg²⁺ or Ca²⁺, or other physiologically acceptable metal in the +2 oxidation state.

10

53. A stabilized radiopharmaceutical composition comprising a compound of claim 51, wherein the stabilizer compound is selected from the group consisting of 1-pyrrolidine dithiocarbamic acid ammonium salt, Sodium diethyldithiocarbamate trihydrate, Sodium dimethyldithiocarbamate hydrate, and combinations thereof.

15

54. A stabilized radiopharmaceutical composition comprising a compound of claim 53, wherein the stabilizer compound is 1-pyrrolidine dithiocarbamic acid ammonium salt.

20

55. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

M is a metal chelator complexed with a radionuclide;

25

N is O, an alpha amino acid, a substituted bile acid, or other linking group;

O is an alpha amino acid, or a substituted bile acid;

P is O, an alpha amino acid, a substituted bile acid, or other linking group; and

30

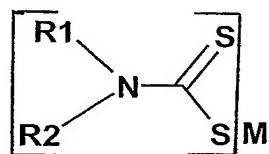
Q is a targeting molecule;

wherein at least one of N, O or P is a substituted bile acid; and

(b) a stabilizer comprising a dithiocarbamate compound.

56. A stabilized radiopharmaceutical composition of claim 55 wherein the

dithiocarbamate compound has the formula:

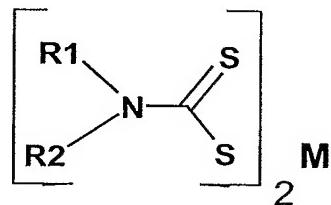


10 wherein R1 and R2 are each independently H; C₁-C₈ alkyl; -OR3, wherein R3 is C₁-C₈ alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

15 wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is H⁺, Na⁺, K⁺, NH₄⁺, N-methylglucamine, or other pharmaceutically acceptable +1 ion.

57. A stabilized radiopharmaceutical composition of claim 55 wherein the dithiocarbamate compound has the formula:

20



25 wherein R1 and R2 are each independently H; C₁-C₈ alkyl; -OR3, wherein R3 is C₁-C₈ alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is Mg²⁺ or Ca²⁺, or other physiologically acceptable metal in the +2 oxidation state.

5 58. A stabilized radiopharmaceutical composition comprising a compound of claim 55, wherein the stabilizer compound is selected from the group consisting of 1-pyrrolidine dithiocarbamic acid ammonium salt, Sodium diethyldithiocarbamate trihydrate, Sodium dimethyldithiocarbamate hydrate, and combinations thereof.

10 59. A stabilized radiopharmaceutical composition comprising a compound of claim 58, wherein the stabilizer compound is 1-pyrrolidine dithiocarbamic acid ammonium salt.

15 60. A stabilized radiopharmaceutical composition of claims 43-59, wherein the metal chelator is selected from the group consisting of DTPA, DOTA, DO3A, HP-DO3A, PA-DOTA, MeO-DOTA, MX-DTPA, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM, MECAM, CMDOTA, PnAO, oxa-PnAO, N,N-dimethylGly-Ser-Cys; N,N-dimethylGly-Thr-Cys; N,N-diethylGly-Ser-Cys; N,N-dibenzylGly-Ser-Cys, N,N-dimethylGly-Ser-Cys-Gly; N,N-dimethylGly-Thr-Cys-Gly ; N,N-diethylGly-Ser-Cys-Gly; and N,N-dibenzylGly-Ser-Cys-Gly.

20 61. A stabilized radiopharmaceutical composition of claims 43-59, wherein the targeting molecule is a targeting peptide.

25 62. A stabilized radiopharmaceutical composition of claim 61, wherein the targeting peptide is selected from the group consisting of LHRH, insulin, oxytocin, somatostatin, NK-1, VIP, Substance P, NPY, endothelin A, endothelin B, bradykinin, interleukin-1, EGF, CCK, galanin, MSH, Lanreotide, Octreotide, Maltose, arginine-vasopressin and analogs and derivatives thereof.

30 63. A stabilized radiopharmaceutical composition of claim 61, wherein the targeting peptide is LHRH or an analog thereof.

35 64. A stabilized radiopharmaceutical composition of claim 61, wherein the targeting molecule is a GRP receptor targeting molecule or an analog thereof.

65. A stabilized radiopharmaceutical composition of claim 64, wherein the GRP receptor targeting molecule is an agonist or a peptide which confers agonist activity.

5 66. A stabilized radiopharmaceutical composition of claim 64, wherein the GRP receptor targeting molecule is bombesin or an analog thereof.

10 67. A stabilized radiopharmaceutical composition of claims 43-59, wherein the radionuclide is selected from the group consisting of ^{99m}Tc , ^{51}Cr , ^{67}Ga , ^{68}Ga , ^{47}Sc , ^{167}Tm , ^{141}Ce , ^{123}I , ^{125}I , ^{131}I , ^{18}F , ^{11}C , ^{15}N , ^{111}In , ^{168}Yb , ^{175}Yb , ^{140}La , ^{90}Y , ^{88}Y , ^{86}Y , ^{153}Sm , ^{166}Ho , ^{165}Dy , ^{166}Dy , ^{62}Cu , ^{64}Cu , ^{67}Cu , ^{97}Ru , ^{103}Ru , ^{186}Re , ^{188}Re , ^{203}Pb , ^{211}Bi , ^{212}Bi , ^{213}Bi , ^{214}Bi , ^{225}Ac , ^{211}At , ^{105}Rh , ^{109}Pd , ^{117m}Sn , ^{149}Pm , ^{161}Tb , ^{177}Lu , ^{198}Au and ^{199}Au and oxides or nitrides thereof.

15 68. A stabilized radiopharmaceutical composition comprising:

(a) a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and

(b) a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

20 69. A stabilized radiopharmaceutical composition comprising:

(a) a metal chelator complexed with a radionuclide;

(b) an optional linking group and a targeting molecule; and

(c) a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

25

70. A stabilized radiopharmaceutical composition of claim 69, wherein the linking group is a hydrocarbon linking group.

30 71. A stabilized radiopharmaceutical composition of claim 70, wherein the linking group is aminovaleric acid.

72. A stabilized radiopharmaceutical composition of claim 69, wherein the stabilizer comprises cysteine or a derivative thereof, mercaptoethanol, or dithiolthreitol, or pharmaceutically acceptable salts thereof.

73. A stabilized radiopharmaceutical composition of claim 72, wherein the stabilizer comprises a cysteine derivative selected from the group consisting of cystamine dihydrochloride, cysteine hydrochloride monohydrate, cysteine ethyl ester hydrochloride, cysteine diethyl ester dihydrochloride, cysteine methyl ester hydrochloride, cysteine dimethyl ester dihydrochloride, cysteinesulfenic acid monohydrate, 5-thio-d-glucose, reduced l-glutathione, and combinations thereof.

74. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

M is a metal chelator complexed with a radionuclide;

N is O, an alpha amino acid, a non-alpha amino acid, or other linking group;

15 O is an alpha amino acid, or a non-alpha amino acid;

P is O, an alpha amino acid, a non-alpha amino acid, or other linking group; and

Q is a targeting molecule;

wherein at least one of N, O or P is a non-alpha amino acid; and

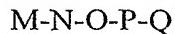
20 (b) a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

75. A stabilized radiopharmaceutical composition of claim 74, wherein the stabilizer comprises cysteine or a derivative thereof, mercaptoethanol, or dithiolthreitol, or pharmaceutically acceptable salts thereof.

76. A stabilized radiopharmaceutical composition of claim 75, wherein the stabilizer comprises a cysteine derivative selected from the group consisting of cystamine dihydrochloride, cysteine hydrochloride monohydrate, cysteine ethyl ester hydrochloride, cysteine diethyl ester dihydrochloride, cysteine methyl ester hydrochloride, cysteine dimethyl ester dihydrochloride, cysteinesulfenic acid monohydrate, 5-thio-d-glucose, reduced l-glutathione, and combinations thereof.

77. A stabilized radiopharmaceutical composition comprising:

(a) a compound of the general formula:



wherein

M is a metal chelator complexed with a radionuclide;

5 N is 0, an alpha amino acid, a substituted bile acid, or other linking group;

O is an alpha amino acid, or a substituted bile acid;

P is 0, an alpha amino acid, a substituted bile acid, or other linking group; and

10 Q is a targeting molecule;

wherein at least one of N, O or P is a substituted bile acid; and

(b) a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

15 78. A stabilized radiopharmaceutical composition of claim 77, wherein the stabilizer comprises cysteine or a derivative thereof, mercaptoethanol, or dithiolthreitol, or pharmaceutically acceptable salts thereof.

20 79. A stabilized radiopharmaceutical composition of claim 78, wherein the stabilizer comprises a cysteine derivative selected from the group consisting of cystamine dihydrochloride, cysteine hydrochloride monohydrate, cysteine ethyl ester hydrochloride, cysteine diethyl ester dihydrochloride, cysteine methyl ester hydrochloride, cysteine dimethyl ester dihydrochloride, cysteinesulfenic acid monohydrate, 5-thio-d-glucose, reduced l-glutathione, and combinations thereof.

25 80. A stabilized radiopharmaceutical composition of claims 68-79, wherein the metal chelator is selected from the group consisting of DTPA, DOTA, DO3A, HP-DO3A, PA-DOTA, MeO-DOTA, MX-DTPA, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM, MECAM, CMDOTA, PnAO, oxa-PnAO, N,N-dimethylGly-Ser-Cys; N,N-dimethylGly-Thr-Cys; N,N-diethylGly-Ser-Cys; N,N-dibenzylGly-Ser-Cys, N,N-dimethylGly-Ser-Cys-Gly; N,N-dimethylGly-Thr-Cys-Gly ; N,N-diethylGly-Ser-Cys-Gly; and N,N-dibenzylGly-Ser-Cys-Gly.

81. A stabilized radiopharmaceutical composition of claims 68-79 wherein the targeting molecule is a targeting peptide.

82. A stabilized radiopharmaceutical composition of claim 81, wherein the targeting peptide is selected from the group consisting of LHRH, insulin, oxytocin, somatostatin, NK-1, VIP, Substance P, NPY, endothelin A, endothelin B, bradykinin, interleukin-1, EGF, CCK, galanin, MSH, Lanreotide, Octreotide, Maltose, arginine-vasopressin and analogs and derivatives thereof.

10 83. A stabilized radiopharmaceutical composition of claim 81, wherein the targeting peptide is LHRH or an analog thereof.

84. A stabilized radiopharmaceutical composition of claim 81, wherein the targeting molecule is a GRP receptor targeting molecule or an analog thereof.

15 85. A stabilized radiopharmaceutical composition of claim 82, wherein the GRP receptor targeting molecule is an agonist or a peptide which confers agonist activity.

20 86. A stabilized radiopharmaceutical composition of claim 82, wherein the GRP receptor targeting molecule is bombesin or an analog thereof.

87. A stabilized radiopharmaceutical composition of claims 73-87, wherein the radionuclide is selected from the group consisting of ^{99m}Tc , ^{51}Cr , ^{67}Ga , ^{68}Ga , ^{47}Sc , ^{167}Tm , ^{141}Ce , ^{123}I , ^{125}I , ^{131}I , ^{18}F , ^{11}C , ^{15}N , ^{111}In , ^{168}Yb , ^{175}Yb , ^{140}La , ^{90}Y , ^{88}Y , ^{86}Y , ^{153}Sm , ^{166}Ho , ^{165}Dy , ^{166}Dy , ^{62}Cu , ^{64}Cu , ^{67}Cu , ^{97}Ru , ^{103}Ru , ^{186}Re , ^{188}Re , ^{203}Pb , ^{211}Bi , ^{212}Bi , ^{213}Bi , ^{214}Bi , ^{225}Ac , ^{211}At , ^{105}Rh , ^{109}Pd , ^{117m}Sn , ^{149}Pm , ^{161}Tb , ^{177}Lu , ^{198}Au and ^{199}Au and oxides or nitrides thereof.

88. A method for stabilizing a radiopharmaceutical composition comprising:

30 (a) combining a radionuclide with a chelator so as to form a radiolabelled complex; and
(b) combining the complex with a stabilizer comprising a water-soluble organic compound containing selenium in the +2 oxidation state.

89. A method of claim 88, wherein the water-soluble compound containing 35 ^{75}Se selenium in the +2 oxidation state is selenomethionine or a derivative thereof.

90. A method of claim 88, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenocysteine or a derivative thereof.

5 91. A method for stabilizing a radiopharmaceutical composition comprising:

(a) combining a radionuclide with a chelator so as to form a radiolabelled complex; and

(b) combining the complex with a stabilizer composition which comprises ascorbic acid or a pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

10 92. A method of embodiment 91 wherein the stabilizer composition further comprises selenomethionine or a derivative thereof.

15 93. A method of claim 91 wherein the stabilizer composition further comprises selenocysteine or a derivative thereof.

94. A method of claim 91 wherein the stabilizer composition further comprises methionine or a derivative thereof.

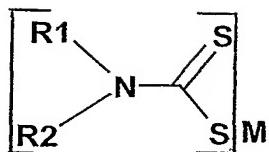
20 95. A method of claim 91 wherein the stabilizer composition further comprises cysteine or a derivative thereof.

96. A method for stabilizing a radiopharmaceutical composition comprising:

25 (a) combining a radionuclide with a chelator so as to form a radiolabelled complex; and

(b) combining the complex with a stabilizer comprising a dithiocarbamate compound.

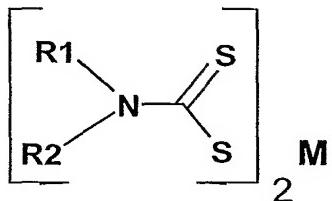
30 97. A method of claim 96 wherein the dithiocarbamate compound has the formula:



wherein R1 and R2 are each independently H, C₁-C₈ alkyl, -OR3 wherein R3 is C₁-C₈ alkyl, or benzyl, either unsubstituted or optionally substituted with water solubilizing groups;
5 or

wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is H⁺, Na⁺, K⁺, NH₄⁺ or other pharmaceutically acceptable +1 ion.

10 98. A stabilized radiopharmaceutical composition of claim 96 wherein the dithiocarbamate compound has the formula:



15 wherein R1 and R2 are each independently H; C₁-C₈ alkyl; -OR3, wherein R3 is C₁-C₈ alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

20 wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is Mg²⁺ or Ca²⁺, or other physiologically acceptable metal in the +2 oxidation state.

25 99. A method of claim 97, wherein the stabilizer compound is selected from the group consisting of 1-pyrrolidine dithiocarbamic acid ammonium salt, sodium diethyldithiocarbamate trihydrate and sodium dimethyldithiocarbamate hydrate, and combinations thereof.

100. A method for stabilizing a radiopharmaceutical composition comprising:

(a) combining a radionuclide with a chelator so as to form a radiolabelled complex; and

(b) combining the complex with a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

5

101. A method of claim 100, wherein the stabilizer comprises cysteine or a derivative thereof, mercaptoethanol, or dithiolthreitol, or pharmaceutically acceptable salts thereof.

10 102. A method of claim 101, wherein the stabilizer comprises a cysteine derivative selected from the group consisting of cystamine dihydrochloride, cysteine hydrochloride monohydrate, cysteine ethyl ester hydrochloride, cysteine diethyl ester dihydrochloride, cysteine methyl ester hydrochloride, cysteine dimethyl ester dihydrochloride, cysteinesulfinic acid monohydrate, 5-thio-d-glucose, reduced 1-glutathione, and combinations thereof.

15

103. A method for stabilizing a radiopharmaceutical composition comprising simultaneously reacting a radionuclide with a chelator and with a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

20 104. A method of claim 103, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenomethionine or a derivative thereof.

105. A method of claim 103, wherein the water-soluble compound containing selenium in the +2 oxidation state is selenocysteine or a derivative thereof.

25

106. A method for stabilizing a radiopharmaceutical composition comprising simultaneously reacting a radionuclide with a chelator and with a stabilizer composition which comprises ascorbic acid or a pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

30

107. A method of claim 106 wherein the stabilizer composition further comprises selenomethionine or a derivative thereof.

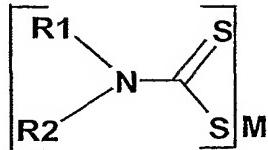
35 108. A method of claim 106 wherein the stabilizer composition further comprises selenocysteine or a derivative thereof.

109. A method of claim 106 wherein the stabilizer composition further comprises methionine or a derivative thereof.

5 110. A method of claim 106 wherein the stabilizer composition further comprises cysteine or a derivative thereof.

10 111. A method for stabilizing a radiopharmaceutical composition comprising simultaneously reacting a radionuclide with a chelator and with a stabilizer comprising a dithiocarbamate compound.

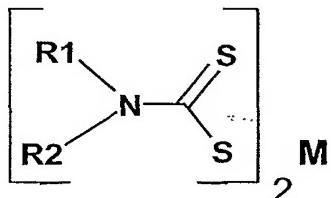
15 112. A method of claim 111 wherein the dithiocarbamate compound has the formula:



20 wherein R1 and R2 are each independently H, C₁-C₈ alkyl, -OR₃, wherein R₃ is C₁-C₈ alkyl, or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is H⁺, Na⁺, K⁺, NH₄⁺ or other pharmaceutically acceptable +1 ion.

25 113. A stabilized radiopharmaceutical composition of claim 111 wherein the dithiocarbamate compound has the formula:



wherein R1 and R2 are each independently H; C1-C8 alkyl; -OR3, wherein R3 is C1-C8 alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

5 wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is Mg²⁺ or Ca²⁺, or other physiologically acceptable metal in the +2 oxidation state.

10 114. A method of claim 112, wherein the stabilizer compound is 1-pyrrolidine dithiocarbamic acid ammonium salt.

115. A method for stabilizing a radiopharmaceutical composition comprising simultaneously reacting a radionuclide with a chelator and with a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

15 116. A method of claim 115, wherein the stabilizer comprises cysteine or a derivative thereof, mercaptoethanol, or dithiolthreitol, or pharmaceutically acceptable salts thereof.

20 117. A method of claim 116, wherein the stabilizer comprises a cysteine derivative selected from the group consisting of cystamine dihydrochloride, cysteine hydrochloride monohydrate, cysteine ethyl ester hydrochloride, cysteine diethyl ester dihydrochloride, cysteine methyl ester hydrochloride, cysteine dimethyl ester dihydrochloride, cysteinesulfenic acid monohydrate, 5-thio-d-glucose, reduced l-glutathione, and combinations thereof.

25 118. A kit for the preparation of a stabilized radiopharmaceutical composition comprising:

(a) a first reagent which comprises a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and

30 (b) a second reagent which comprises a stabilizer comprising a water-soluble organic compound containing selenium in the +2 oxidation state.

119. A kit of claim 118 wherein the water-soluble compound containing selenium in the +2 oxidation state is selenomethionine or a derivative thereof.

120. A kit of claim 118 wherein the water-soluble compound containing selenium in the +2 oxidation state is selenocysteine or a derivative thereof.

5 121. A kit for the preparation of a stabilized radiopharmaceutical composition comprising:

- (a) a first reagent which comprises a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and
 - (b) a second reagent which comprises a stabilizer composition which
- 10 comprises ascorbic acid or a pharmaceutically salt thereof, gentisic acid or a pharmaceutically salt thereof, human serum albumin, and benzyl alcohol.

122. A kit of claim 121 wherein the stabilizer composition further comprises selenomethionine or a derivative thereof.

15 123. A kit of claim 121 wherein the stabilizer composition further comprises selenocysteine or a derivative thereof.

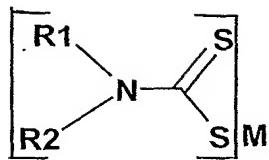
20 124. A kit of claim 121 wherein the stabilizer composition further comprises methionine or a derivative thereof.

125. A kit of claim 121 wherein the stabilizer composition further comprises cysteine or a derivative thereof.

25 126. A kit for the preparation of a stabilized radiopharmaceutical composition comprising:

- (a) a first reagent which comprises a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and
 - (b) a second reagent which comprises a stabilizer comprising a
- 30 dithiocarbamate compound.

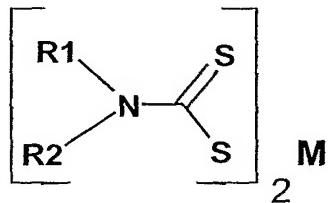
127. A kit of claim 126 wherein the dithiocarbamate compound has the formula:



wherein R1 and R2 are each independently H, C₁-C₈ alkyl, -OR₃, wherein R₃ is C₁-C₈ alkyl, or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is H⁺, Na⁺, K⁺, NH₄⁺ or other pharmaceutically acceptable +1 ion;

10 or



wherein R1 and R2 are each independently H; C₁-C₈ alkyl; -OR₃, wherein R₃ is C₁-C₈ alkyl; or benzyl, either unsubstituted or optionally substituted with water solubilizing groups; or

wherein R1, R2, and N combined form 1-pyrrolidinyl-, piperidino-, morpholino-, 1-piperazinyl-; and M is Mg²⁺ or Ca²⁺, or other physiologically acceptable metal in the +2 oxidation state.

128. A kit for the preparation of a stabilized radiopharmaceutical composition comprising:

- (a) a first reagent which comprises a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and
- (b) a second reagent which comprises a stabilizer comprising a water-soluble compound containing sulfur in the +2 oxidation state.

129. A kit of claim 128 wherein the stabilizer comprises cysteine or a derivative thereof, mercaptoethanol, or dithiolthreitol, or pharmaceutically acceptable salts thereof.

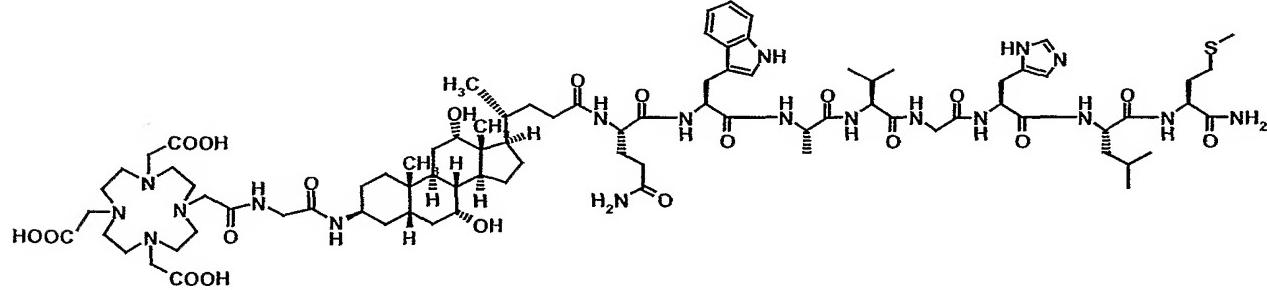
130. A kit of claim 129 wherein the stabilizer comprises a cysteine derivative selected from the group consisting of cystamine dihydrochloride, cysteine hydrochloride monohydrate, cysteine ethyl ester hydrochloride, cysteine diethyl ester dihydrochloride, cysteine methyl ester hydrochloride, cysteine dimethyl ester dihydrochloride, cysteinesulfinic acid monohydrate, 5-thio-d-glucose, reduced 1-glutathione, and combinations thereof.

10 131. A kit for the preparation of a stabilized radiopharmaceutical composition comprising:

(a) a first reagent which comprises a diagnostic or therapeutic radionuclide, optionally complexed to a chelator; and

15 (b) a second reagent which comprises a stabilizer comprising a comprising a water-soluble compound containing sulfur in the +2 oxidation state.

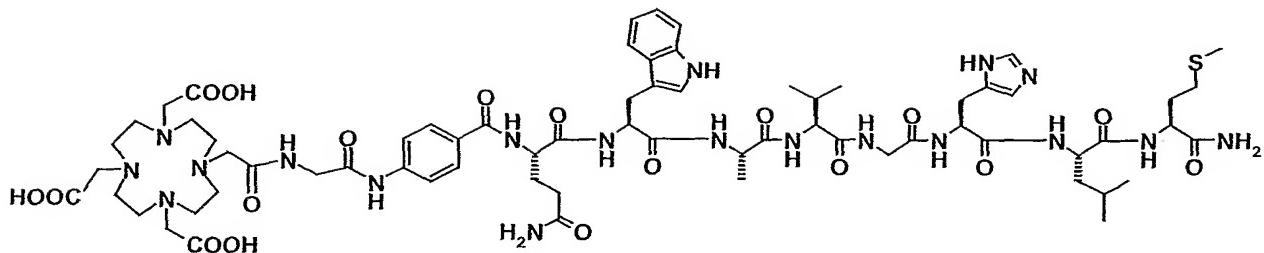
132. A stabilized radiopharmaceutical composition comprising a compound of the formula:



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and a stabilizing composition comprising Ascorbic Acid, Gentisic acid, Human Serum Albumin, Benzyl Alcohol, and an amino acid selected from the group consisting of cysteine, methionine, or Selenomethionine.

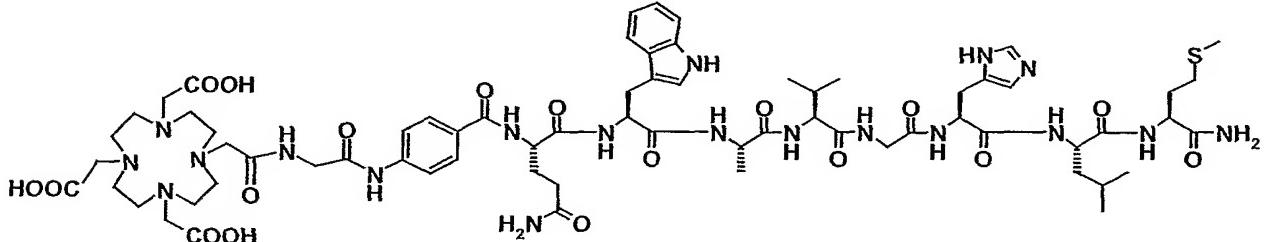
25 133. A stabilized radiopharmaceutical composition comprising a compound of the formula:



5 and a stabilizing composition comprising Ascorbic Acid, Gentisic acid, Human Serum
Albumin, Benzyl Alcohol, and an amino acid selected from the group consisting of cysteine,
methionine, or Selenomethionine.

134. A kit for the preparation of a stabilized radiopharmaceutical composition
10 comprising:

(a) a first reagent which comprises a compound of the formula:



and a water-soluble organic compound containing selenium in the +2 oxidation state; and

15 (b) a second reagent which comprises ascorbic acid or a pharmaceutically
salt thereof, sodium chloride, EDTA, and benzyl alcohol.

135. A kit of claim 134, wherein the compound containing selenium in the +2 oxidation state is selenomethionine.

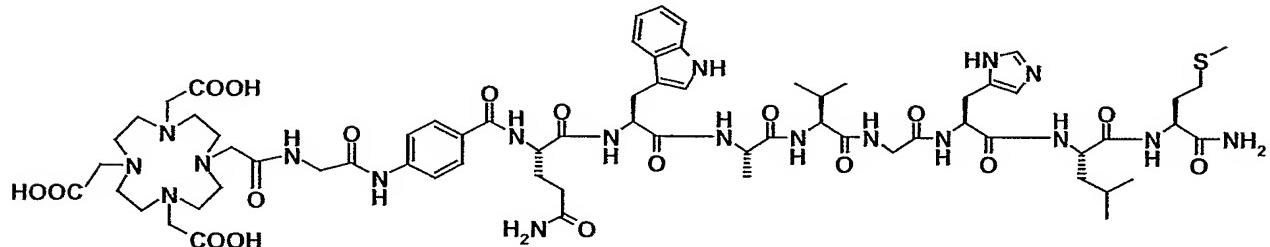
136. A kit of claim 135, wherein the first reagent further comprises a radionuclide.

137. A kit of claim 136, wherein the radionuclide is selected from the group consisting of ^{177}Lu , ^{111}In , and ^{90}Y .

138. A kit of claim 137, wherein the radionuclide is ^{177}Lu .

139. A kit for the preparation of a stabilized radiopharmaceutical composition comprising:

- (a) a first reagent which comprises a compound of the formula:



and a water-soluble organic compound containing selenium in the +2 oxidation state; and

- (b) a second reagent which comprises ascorbic acid or a pharmaceutically salt thereof, sodium chloride, EDTA, and benzyl alcohol.

140. A kit of claim 139, wherein the compound containing selenium in the +2 oxidation state is selenomethionine.

15 141. A kit of claim 140, wherein the first reagent further comprises a radionuclide.

142. A kit of claim 141, wherein the radionuclide is selected from the group consisting of ^{177}Lu , ^{111}In , and ^{90}Y .

20 143. A kit of claim 137, wherein the radionuclide is ^{177}Lu .

144. A method of increasing recovery of radioactivity from a reaction that produces a radiopharmaceutical composition, comprising adding benzyl alcohol to a reaction mixture that produces the radiopharmaceutical composition.

25 145. A method of increasing recovery of radioactivity from a reaction that produces a radiopharmaceutical composition comprising:

- (a) reacting a radionuclide with a chelator to form a radiolabeled chelate;
- (b) reacting the radiolabeled chelate with a stabilizer solution comprising

30 benzyl alcohol.

146. A method of claim 145, wherein the stabilizer solution further comprises ascorbic acid or a pharmaceutically acceptable salt thereof.

147. A method of claim 145, wherein the stabilizer solution further comprises
5 EDTA.

148. A method of reducing one or more oxidized methionine residues in a radiopharmaceutical composition comprising reacting the radiopharmaceutical composition with cysteine.

10 149. A method of reducing one or more oxidized methionine residues in a radiopharmaceutical composition comprising reacting the radiopharmaceutical composition with dithiolthreitol.

15 150. A method of reducing one or more oxidized methionine residues in a radiopharmaceutical composition comprising reacting the radiopharmaceutical composition with mercaptoethanol.

20 151. A method of any of claims 148-150, wherein the radiopharmaceutical composition comprises a compound having the formula of Compound A.

152. A method of any of claims 148-150, wherein the radiopharmaceutical composition comprises a compound having the formula of Compound B.

25 153. A method of reducing interference from metallic contaminants in a reaction mixture for the preparation of a radiopharmaceutical comprising reacting the mixture with a dithiocarbamate.

154. The method of claim 153, wherein the dithiocarbamate is PDTC.

30 155. A method of improving yield of a desired radiopharmaceutical, comprising adding a dithiocarbamate to the reaction mixture that produces the radiopharmaceutical.

156. The method of claim 155, wherein the dithiocarbamate is PDTC.